UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION,
PESTICIDES
AND TOXIC
SUBSTANCES

September 30, 2009

MEMORANDUM

Subject: Efficacy Review for PeraDox HC Solution Part A; EPA File Symbol 84545-U; DP Barcode: 363855

From: Tajah L. Blackburn, Ph.D., Microbiologist
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9/30/09

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Applicant: sBioMed, LLC
1272 South 1380 West
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Formulation from the Label:

(Part A)

Active Ingredient	% by wt.
Silver	0.03 %
Other Ingredients	99.97 %
Total	100.00 %

(Part B)

Active Ingredients	% by wt.
Hydrogen Peroxide	22.0 %
Peroxyacetic Acid	15.0 %
Other Ingredients	63.0 %
Total	100.00 %

I BACKGROUND

The product, PeraDox HC Solution Part A (EPA File Symbol 84545-U), is a new product. The product is combined with an activator, PeraDox HC Activator Solution Part B, prior to use. The activated product is for use as a sporicide and disinfectant (bactericide, tuberculocide, virucide) on hard, non-porous surfaces in household, commercial, institutional, food preparation, animal care, and hospital or medical environments. The study to support claims against Poliovirus Type 1 Strain CHAT was conducted at Brigham Young University, Microbiology and Molecular Biology Laboratory, located in Provo, UT.

This data package contained letters from the applicant's representative to EPA (dated March 13, 2009 and June 30, 2009), EPA Form 8570-1 (Application for Pesticide), EPA Form 8570-4 (Confidential Statement of Formula), one study (MRID 477904-01), Statements of No Data Confidentiality Claims, and the proposed label.

Note: This data package also contained EPA Form 8570-4 (Confidential Statement of Formula) and the proposed label for the activator component, PeraDox HC Activator Solution Part B.

Note: EPA Form 8570-4 (Confidential Statement of Formula) contains Confidential Business Information. Data or information claimed by the applicant to be FIFRA confidential has not been included in this report.

II USE DIRECTIONS

The activated product is designed for use on hard, non-porous surfaces, including: activity centers, appliances, baskets, bassinets, bathtubs, bed rails, cabinets, carts, cellular phones, chairs, child car seats, computer keyboards, counter tops, cribs, desks, diaper changing tables, diaper pails, door handles, doorknobs, drain boards, drawer pulls, examination tables, faucet fixtures, floors, hampers, handles, incubators, IV poles, light switch covers, lighting fixtures, mirrors, pails, pans, physical therapy equipment, play chairs and tables, playpens, remote controls, scales, sinks, stools, strollers, shower stalls, showers, stretchers, tables, telephones, toilets, toy boxes, toys, walls, and windowsills. The proposed label indicates that the activated product may be used on hard, non-porous surfaces including: finished woodwork, Formica, glazed ceramic, glazed enamel, glazed porcelain, glazed tile, metal, plastic, sealed granite, sealed limestone, sealed marble, sealed slate, sealed stone, sealed terra cotta, sealed terrazzo, stainless steel, upholstery, and vinyl. Directions on the proposed label provide the following information regarding preparation and use of the product:

> As a disinfectant: Pre-clean heavily soiled surfaces prior to application. Combine PeraDox HC Solution Part A with PeraDox HC Activator Solution Part B as instructed on the proposed label. Thoroughly apply the solution to surfaces using a spray, mop, cloth, or sponge method, covering the surface until wet. Allow the product to remain on the surface to dry or for 3 minutes. For clean-up, rinse the surface with a clean cloth or sponge several times with potable water.

III AGENCY STANDARDS FOR PROPOSED CLAIMS

Virucides

The effectiveness of virucides against specific viruses must be supported by efficacy data that simulates, to the extent possible in the laboratory, the conditions under which the product is intended to be used. Carrier methods that are modifications of either the AOAC Use-Dilution Method (for liquid disinfectants) or the AOAC Germicidal Spray Products as Disinfectants Method (for spray disinfectants) must be used. To simulate in-use conditions, the specific virus to be treated must be inoculated onto hard surfaces, allowed to dry, and then treated with the product according to the directions for use on the product label. One surface for each of 2 different product lots of disinfectant must be tested against a recoverable virus titer of at least 10^4 from the test surface for a specified exposure period at room temperature. Then, the virus must be assayed by an appropriate virological technique, using a minimum of four determinations per each dilution assayed. Separate studies are required for each virus. The calculated viral titers must be reported with the test results. For the data to be considered acceptable, results must demonstrate complete inactivation of the virus at all dilutions. When cytotoxicity is evident, at least a 3-log reduction in titer must be demonstrated beyond the cytotoxic level.

IV SYNOPSIS OF SUBMITTED EFFICACY STUDY

1. MRID 477904-01, Virucidal Efficacy of PeraDox on Poliovirus Type 1 Strain CHAT, by Byron Murray, PhD. Study Completion Date—December 8, 2007. Report Number sb1207-00-01.

The study was conducted using Poliovirus Type 1 Strain CHAT (purchasing source not identified) using Vero cells (purchasing source not identified) as the host system. Three lots (Lot Nos. 23, 36, and 39) were tested using DIS/TSS-7, ASTM E1052-96 Standard Test Method for Efficacy of Antimicrobial Agents Against Viruses in Suspension, and ASTM E1053-97 Standard Test Method for Efficacy of Virucidal Agents Intended for Inanimate Environmental Surfaces. Carriers were prepared using 0.1 ml of virus suspension, and allowed to dry in a containment hood. Following drying, 1 ml of PeraDox to cover each carrier and incubated for 3 minutes at room temperature. Following exposure, virus and test solution were removed from the carriers and placed into neutralizer. Four wells per dilution were tested. In another method, 100 µl of the virus pool was added to each of 9 treated slides. Slides were air dried at room temperature for 26 minutes. Peradox, at 1ml, was added to each slide for either 1 minute or 3 minutes. Following treatment, samples were diluted with DMEM2 and titered for PFU in 24-welled plates of Vero cells with 1% methylcellulose overlay in DMEM2. Cells were finally fixed with 10% formalin, stained with 1% crystal violet after 4 days and the PFUs enumerated. Controls were included for carrier counts, and neutralization confirmation.

V RESULTS

Virucidal Efficacy of PeraDox in Solution
Lot: 23 Manufactured on 4/10/07

Assay Date: April 24, 2007

The average virus control titer was 7.0×10^6 PFU/ml.
No infectious virus i.e. no plaques could be detected after PeraDox exposure for 3 minutes
The sensitivity of the assay was <5.0 PFU/ml.
The log reduction by PeraDox was 5.2 log.
The neutralizer reduced the virus titer by 0.68 log.
Neutralized PeraDox reduced the virus titer by 0.24 log.
No toxicity was seen with Peradox undiluted or at 10^{-2} dilution, but was at 10^{-1} dilutions.
Peradox + neutralizer at the 10^{-1} dilution was not toxic.

Assay Date: April 26, 2007

The average virus control titer was 5×10^7 PFU/ml.
No infectious virus i.e. no plaques could be detected after PeraDox exposure for 3 minutes
The sensitivity of the assay was <5.0 PFU/ml.
The log reduction by PeraDox was 5.3 log.
Neutralized PeraDox reduced the virus titer by 0.07 log.
No toxicity was seen with Peradox undiluted or when mixed with the neutralizer and titered undiluted or at 10^{-1} dilution.

Assay Date: May 1, 2007

The average virus control titer was 1.1×10^7 PFU/ml.
No infectious virus i.e. no plaques could be detected after PeraDox exposure for 1, 2, 3 minutes. Plaques were seen undiluted at 30 seconds.
The sensitivity of the assay was <1.0 PFU/ml.
The log reduction by PeraDox was 5.3 log after 1, 2 and 3 minutes after exposure. The log reduction after 30 seconds of exposure was 4.0 log.
Neutralized PeraDox reduced the virus titer by 0.08 log.
PeraDox was not toxic at the 10^{-1} dilution or any other dilution assayed when mixed with the neutralizer.

Virucidal Efficacy of PeraDox on Carriers

Lot 36 Manufactured 5/21/07
Assayed Date: July 18, 2007

The average dried virus control titer was 1.7×10^6 PFU/ml.
Plaques were seen in undiluted samples of PeraDox –treated carriers the same as for the assay of July 17, 2007. Eight week-old PeraDox and activator were used in both assays. These are the only times plaques were seen in carriers or in solution after 1 or 3 minutes of PeraDox exposure.
The sensitivity of the assay was 1-12 PFU/ml.
The Log reduction of PFU was 3.2 logs (5.0 logs with fresh PeraDox).
No toxicity was seen with PeraDox or neutralizer in any of the 24 exposed cultures used in the assay.

Lot 36 Manufactured 5/21/07
Assayed Date: July 18, 2007

The average dried virus control titer was 1.6×10^6 PFU/ml.
Plaques were seen in undiluted samples of PeraDox –treated carriers.
Eight week-old PeraDox and activator were used in this assay. This is the first time plaques were seen in carriers or in solution after 1 or 3 minutes of exposure.
The sensitivity of the assay was 1-12 PFU/ml.
The Log reduction of PFU was 3.1 logs (5.1 logs with fresh PeraDox).
No toxicity was seen with PeraDox or neutralizer in any of the 24 exposed cultures used in the assay.

Lot 36 Manufactured 5/21/07
Assay Date: June 12, 2007
The average virus control titer in samples recovered in DMEM2 was > 3.4 logs and >5.0 logs recovered in neutralizer.
No infectious virus i.e. plaques could be detected after PeraDox exposure for 3 minutes.
The sensitivity of the assay was 1-12 PFU/ml.
The Log reduction of PFU recovered in DMEM was >2.3 and was >3.9 when recovered in neutralizer.
No toxicity was seen with PeraDox or neutralizer in any of the 12 exposed cultures used in the assay.

Lot Not specified
Assay Date: June 7, 2007

The average dried virus control titer was 3.5×10^4 PFU/ml.
No infectious virus i.e. plaques could be detected after PeraDox exposure for 3 minutes.
The sensitivity of the assay was 1-12 PFU/ml.
The reduction of PFU titer was 3.4 logs.
In neutralizer control carriers, the virus titer also increased from 3.5×10^4 to 1.0×10^5 PFU/ml, an increase of 0.5 logs.
No toxicity was seen with PeraDox or neutralizer in any of the 16 exposed cultures used in the assay.

Lot Not specified
Assay Date: June 5, 2007

The average dried virus control titer was 3.4×10^4 PFU/ml.
No infectious virus i.e. plaques could be detected after PeraDox exposure for 3 minutes.
The sensitivity of the assay was 1-12 PFU/ml.
The reduction of PFU titer was 3.4 logs.
In neutralizer control carriers, the virus dropped slightly to 3.2×10^4 PFU/ml, a change of 0.4 logs.
No toxicity was seen with PeraDox or neutralizer in any of the 16 exposed cultures used in the assay.

Lot Not specified
Assay Date: May 29, 2007

The average dried virus control titer was 3.1×10^3 PFU/ml.
No infectious virus i.e. plaques could be detected after PeraDox exposure for 3 minutes.
The sensitivity of the assay was 1-12 PFU/ml.
The reduction of PFU titer was >2.4 logs.
No toxicity was seen with PeraDox or neutralizer in any of the 16 exposed cultures used in the assay.

Lot 39 Manufactured on 5/29/07
Assay Date: August 22, 2007

The average dried virus control titer was 3.2×10^5 PFU/ml.
No infectious virus i.e. no plaques could be detected after PeraDox exposure for either 1 minute or 3 minutes.
The sensitivity of the assay was 1-12 PFU/ml.
The log reduction in PFU was >4.4 to 5.5 logs at both 1 minute and 3 minutes of PeraDox exposure.
No toxicity was seen with PeraDox or neutralizer in any of the 16 exposed cultures in the assay.

IV CONCLUSIONS

1. The submitted efficacy data (MRID 477904-01) **do not support** the use of the product, PeraDox, as a disinfectant with virucidal activity against Poliovirus Type 1 Strain CHAT on hard, non-porous surfaces for a 3-minute contact time. The data provided was unclear regarding (1) preparation of the test substances [activated or non-activated]; (2) test concentration; (3) the minimum determinations per each dilution (the minimum is 4); (4) the ID_{50} values calculated for each assay; (5) The test results shall be reported as the reduction of the virus titer by the activity of the germicide (ID-50 of the virus control less the ID-50 of the test system), expressed as $\log_{10}$ and calculated by a statistical method (Reed and Muench, 1938; Litchfield and Wilcoxon, 1949; as examples).

Furthermore, a typical laboratory report of a **single** test with **one** virus (recovered from a treated surface) involving a tissue culture, therefore, would include the details of the methods employed and the information in the provided tables.

DIS/TSS-7 Tables

Virucides Test Results (Example of Data Presentation)

Table 1 - Test Results

Dilution of Virus	Virus - Disinfectant*	Virus - Control*	Cytotoxic-Control
10^{-1}	TTTT	++++	TTTT
10^{-2}	TTTT	++++	TTTT
10^{-3}	T000	++++	T000
10^{-4}	0000	++++	0000
10^{-5}	0000	++++	0000
10^{-6}	0000	+++0	0000
10^{-7}	0000	+000	0000
10^{-8}	0000	0000	0000

*Recovery of virus from surfaces demonstrated by cytopathogenic effect, fluorescent antibody, plaque count, animal' response, or other recognized acceptable technique.

Note: T = toxic; + = virus recovered; 0 = no virus recovered.

Table II-Calculation of the Tissue Culture Infective $Dose_{50}$ ($TCID_{50}$)

Values				Accumulated Values			
Virus Dilution Inoculated	No. Infected / No. Inoculated	No. Infected	No. Not Infected	No. Infected	No. Not Infected	No. Infected / No. Inoculated	Percent Infected
10^{-1}	4/4	4	0	24	0	24/24	100
10^{-2}	4/4	4	0	20	0	20/20	100
10^{-3}	4/4	4	0	16	0	16/16	100
10^{-4}	4/4	4	0	12	0	12/12	100
10^{-5}	4/4	4	0	8	0	8/8	100
10^{-6}	3/4	3	1	4	1	4/5	80
10^{-7}	1/4	1	3	1	4	1/5	20
10^{-8}	0/4	0	4	0	8	0/8	0

$TCID_{50} = 10^{6.5}$

Table III-Calculation of the Tissue Culture Lethal Dose$_{50}$ (TCLD$_{50}$)

Values				Accumulated Values			
Virus Dilution Inoculated	No. Toxic / No. Inoculated	No. Toxic	No. Not Toxic	No. Toxic	No. Not Toxic	No. Toxic / No. Inoculated	Percent Toxic
10^{-1}	4/4	4	0	9	0	9/9	100
10^{-2}	4/4	4	0	5	0	5/5	100
10^{-3}	1/4	1	3	1	3	1/4	25
10^{-4}	0/4	0	4	0	7	0/7	0
10^{-5}	0/4	0	4	0	11	0/11	0
10^{-6}	0/4	0	4	0	15	0/15	0
10^{-7}	0/4	0	4	0	19	0/19	0
10^{-8}	0/4	0	4	0	23	0/23	0

$TCID_{50} = 10^{2.7}$

Therefore: Virus inactivation = $TCID_{50} - TCLD_{50} = 10^{3.8}$ log $_{10}$

Claims for virucidal activity for a product must be restricted to those viruses which have actually been tested.

Additionally, in the situations in which neutralization contributed log reduction, did the final log reductions include an adjustment for the neutralization efficacy?

VII RECOMMENDATIONS

1. The proposed label claims are unacceptable regarding the use of the product PeraDox, as a virucide against Poliovirus Type 1 Strain CHAT on hard, non-porous surfaces at a contact time of 3 minutes. The issues stated in the Conclusion must be resolved before this claim is granted.

2. When claims are accepted, the contact must be stated as "3 minutes" or a number consistent with efficacy testing. The statement "remain on the surface to dry" is inadequate due to variability with surface types, temperatures, and relative humidity.